## REMARKS

Please consider this paper as a petition for extension of time.

Please charge the required fees to have the petition and amendment entered to our deposit account 500687.

Claims 36-58 are pending. All claims read on the elected species of Group I. The election of Group I is made without traverse. Applicant retains the right to pursue the subject matter of the non-elected Groups in divisional applications. All claim amendments have been made without prejudice.

Basis for new claims 36-58 can be found in the originally filed application including as follows:

new claims 36 and 37 at previous claim 1;

new claim 38 at previous claim 2;

new claim 39 at previous claim 3;

new claim 40 at previous claim 4;

new claim 41 at previous claim 5;

new claim 42 at previous claim 6;

new claim 43 at previous claim 7;

new claim 44 at previous claim 8;

new claim 45 at previous claim 9;

new claim 46 at previous claim 10;

new claim 47 at page 5, second paragraph;

new claims 48 and 49 at page 5, first paragraph;

new claim 50 at page 4, last paragraph;

new claim 51 at page 5, second paragraph;

new claim 52 at page 11, second paragraph;

new claims 53 and 54 at page 6, first paragraph, and page 11, first and second paragraphs;

new claim 55 at previous claim 1 and page 7, third paragraph;

new claim 56 at page 7, third paragraph;

new claim 57 at page 9, second paragraph; and

new claim 57 at page 5, second paragraph.

No new matter has been added. No claims have been amended to overcome prior art. Claim 36 recites at least the breadth of original claim 1 in the parent PCT application and, thus, the claim breadth has not been narrowed. The method claims have been amended to recite active steps. The full doctrine of equivalents applies to each claim element.

The rejection of claims 1-3 and 5-10 (now claims 36-39 and 41-46) under 35 U.S.C. § 102(b) as being anticipated by EP 0 080 862 (Grimmett) is respectfully traversed. The claimed invention is not anticipated by Grimmett for the following reasons.

Claims 36-57 recite "extruding the sieved mixture with a granulation liquid comprising water to obtain a wet extruded mass."

Grimmett excludes the addition of water during the extruding step. See page 1, last line of Grimmett, which states that "a non-hygroscopic water soluble binder" should be used. Grimmett, at page 2, lines 8 to 12, further discloses that the employed materials should have low free moisture content, should be pre-dried, and "advantageously an edible desiccant may be incorporated in the composition." A desiccant is a "drying agent," which is the opposite of adding water. Grimmett at page 2 then goes on to provide a list of suitable solvents for use when forming the extrudate and among the many standard solvents mentioned (methanol, ethanol, acetone, methyl acetate, etc.) water is not included. Grimmett further teaches on page 3, lines 7 to 10, that the formulation process should be carried out under a dry atmosphere. These teachings in Grimmett require that no water be added during the extrusion process.

In contrast, the claimed invention requires the addition of water so that a wet mass is produced during the extrusion step.

Applicant respectfully submits that the Examiner's statement on page 3 of the Office Action that the "dichloromethane" used in Example 1 of Grimmett is an aqueous solution is respectfully traversed. Dichloromethane is clearly an organic solvent, not an aqueous solution. Aqueous solutions require water. Example 1 of

Grimmett teaches to use "anhydrous" silicic acid, which is free of water. Furthermore, Grimmett in Example 1 teaches that the extruded mass produces a "dry powder mix," without a drying step. See page 5, last paragraph of Grimmett. The drying step in Example 1 of Grimmett referred to by the Examiner is after the "dry powder mix" is formed by the extrusion step. In contrast, in the claimed invention water is added to form a wet extruded mass (not a dry power mix), and the dry particles are formed by a drying step. Grimmett clearly teaches against using water in the extrusion process.

The only time Grimmett teaches to use water is when administering the dry particles to a patient. The dry particles are suspended in water to form a solution to be consumed by a patient. See page 3, lines 15-23 of Grimmett.

In view of the differences between Grimmett and the claimed invention, withdrawal of the Section 102 rejection is respectfully requested.

The rejection of claims 1 and 4 (now claims 36 and 40) under 35 U.S.C. 103(a) as being unpatentable over Grimmett in view of U.S. Published Patent Application No. 2002/0006433 (Davidson) is respectfully traversed. The claimed invention is not taught or suggested by the theoretical combination of references for the following reasons.

As discussed above, the claimed invention requires the use of water in the extrusion step to produce a wet mass, and Grimmett teaches away from using water in the extrusion step. Davidson does not provide the deficiencies of Grimmett.

Davidson does not teach or suggest adding water to a mixture of amoxicillin trihydrate and sugar so that a wet mass is extruded during an extruding step. Thus, the combination of Grimmett and Davidson teaches to avoid water during the extrusion step, which is in a direction away from the claimed invention. For this reason alone, the Section 103 rejection should be withdrawn.

A major problem associated with conventional amoxicillin granules is that they agglomerate and do not form a smooth suspension upon reconstitution, and excipients, such as lubricants, thickeners, suspension agents, etc. are required.

The present invention provides a process for the production of a stable

amoxicillin granulate that is more adapted for the use in paediatric and geriatric patients, which does not require the use of excipients and provides a smooth suspension upon reconstitution. Such a product providing a smooth suspension on reconstitution clearly improves the compliance of patients in taking a medicament, especially if the medicament is taken in larger amounts as is often required in the field of antibiotics.

The present invention provides a water-based extrusion process followed by sieving, drying and homogenization steps. This process generates small-size amoxicillin particles while at the same time avoiding formation of agglomerates and the so produced granulate forms a smooth suspension upon reconstitution with water, as can be seen from Fig. 1 in the present specification.

The effect of large size particles on oral texture and palatability in suspensions is an issue which has been addressed in various examinations, e. g. Tyle, "Effect of size, shape and hardness of particles in suspension on oral texture and palatability," Acta Psychologica 84 (1993) pp. 111-118, copy filed herewith and listed on the attached PTO Form/SB08. Tyle teaches that the characteristics of particles in suspension can cause a problem in drug development due to a lack of compliance of patients if the particles in suspension are too large. If the suspension contains a considerable amount of agglomerates or big sized particles the suspension effects a gritty, very unpleasant taste on ingestion. See page 118, last paragraph of Tyle. Tyle does not teach or suggest how to make particles free of agglomerates or big sized particles.

The novel wet process of the present invention surprisingly provides a granulate wherein the particles of amoxicillin contained therein are of a specific small particle size and are free of agglomeration. This granulate has the ability to decompose to fine particles of micronized amoxicillin trihydrate, which results in a smooth suspension on reconstitution with water. The size of micronized amoxicillin trihydrate particles in the aqueous suspension obtained after reconstitution exhibits a small range of less than 100 µm, with the majority of particles being within the range of 1 to 30 µm. See page 9, second paragraph of the present specification. The granulate of the present invention, which lacks large-sized amoxicillin

particles, thus solves the problem of preventing grittiness on the sensitive human tongue upon ingestion.

In view of the differences between the claimed invention and the theoretical combination of references, and the advantages of the claimed invention, withdrawal of the Section 103 rejection is respectfully requested.

The following U.S. patent applications have common ownership and at least one common inventor: 12/374,095 and 12/595,833. Entry of this information disclosure statement is respectfully requested.

In view of all of the rejections of record having been addressed, it is believed that the application is in condition for allowance and Notice to that effect is respectfully requested.

Respectfully submitted,

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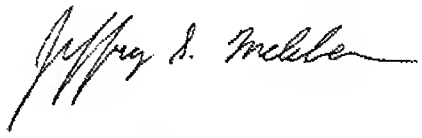

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